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PYLORIC MOTOR FUNCTION DURING EMPTYING OF A LIQUID MEAL FROM THE STOMACH IN THE CONSCIOUS PIG

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SUMMARY

1. In six conscious pigs antral, pyloric and duodenal pressures were recorded with a 5·5 cm sleeve sensor and multiple perfused side holes. The manometric assembly was positioned by dual point transmucosal potential difference measurement. Gastric emptying was measured by drainage of the proximal duodenum through a Thomas cannula. Pressures were correlated with emptying of ingested radiolabelled 5% dextrose. Alteration of emptying was produced by infusion into the more distal duodenum of nutrient and non-nutrient solutions of differing osmolalities.

2. Motor activity of the pylorus and antrum was stimulated by ingestion and modulated by intraduodenal infusion. Duodenal infusion of normal saline was associated with antro-pyloric pressure waves and rapid emptying of the ingested liquid. Duodenal infusion of dextrose, fatty acid, amino acids and hyperosmolar saline was associated with stimulation of isolated pyloric pressure waves, suppression of antral pressure waves and slowing of gastric emptying.

3. The dose–response relationship of these effects was investigated using varying rates of intraduodenal dextrose infusions. The emptying rate of the ingested liquid was inversely related to the rates of delivery of dextrose to the duodenum, directly related to the rate of antro-pyloric pressure waves and inversely related to the rate of isolated pyloric pressure waves.

4. Clearly defined episodes of pulsatile flow produced slightly more than half of the total emptying that occurred. This pulsatile flow was intimately associated in time with antro-pyloric pressure waves. Sequences of isolated pyloric pressure waves were associated with near cessation of emptying. When there were periods of absent pyloric antral pressure waves, flow rates intermediate between the rapid emptying of pulsatile flow during antro-pyloric pressure waves and the near cessation of flow during isolated pyloric pressure waves occurred.

5. The findings suggest a major role for the pylorus in the control of emptying of liquids from the stomach, both as a component of an antro-pyloric peristaltic pump and as a resistor to transpyloric flow during nutrient and hyperosmolar stimulation of duodenal receptors.

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INTRODUCTION

The motor mechanisms involved in the control of gastric emptying are becoming better understood as measurement methods improve. In the mid-1970s a two-component model of the motor events of gastric emptying was proposed, which assigned separate roles to the proximal and distal stomach (Kelly, 1980). In this model, the proximal stomach was assigned a primary role for receipt and storage of food and the control of gastric emptying of liquids. The concept was based mainly upon the effect of various gastric resections or proximal gastric vagotomy (Wilbur & Kelly, 1973; Wilbur, Kelly & Code, 1974). Retention, grinding and propulsion of large-sized particles were functions assigned to the distal stomach.

More recent observations have shown that a two-component model cannot explain all aspects of gastric emptying and that several mechanisms exist which can each modify emptying substantially. Proposed mechanisms include proximal gastric tone, antral peristalsis, pyloric resistance, duodenal contractions, antro-duodenal co-ordination (Meyer, 1987) and the mid-gastric band (Moore, Dubois, Christian, Elgin & Alazraki, 1979). The relative importance of these mechanisms and specifically the role of the pylorus is controversial. Recently the sleeve sensor has been adapted for pyloric manometry and has been used to record effectively the pyloric motor responses to stimuli that retard gastric emptying in humans (Heddle, Dent, Toouli & Read, 1988*a*). The sleeve sensor, by recording the highest pressure generated at any point along its length (Dent, 1976), avoids undermeasurement of sphincter motility that can occur with displacement of a focal sensor from the mobile narrow pylorus (Heddle *et al.* 1988*a*).

The aim of this study was to examine the relationship of pyloric motor function to transpyloric flow of liquids, in order to investigate the importance of pyloric control of gastric emptying. Pyloric motility has been undertaken in animals as the animal preparation allows precise temporal correlation of trans-pyloric flow with gastro-duodenal motility. Further, the establishment of the animal preparation permits experimental manipulations that are not possible in humans. The studies were performed on awake unsedated animals to avoid any influences of general anaesthesia on motor function.

Preliminary results of this work have been published in abstract form (Treacy, Jamieson, Dent, Akkermans, Heddle & Landers, 1988).

METHODS

Surgical preparation

The Kangaroo Island pig has been found to be a suitable animal model for use in biomedical research (McIntosh & Pointon, 1981). Six female Kangaroo Island pigs (weights 34–55 kg), aged 5 months, underwent operation under general anaesthesia (halothane/nitrous oxide), at which a modified Thomas cannula was inserted into the duodenum, 5 cm distal to the pylorus. A second cannula was inserted in the gastric body 10–15 cm proximal to the pylorus (three pigs) or the cervical oesophagus (three pigs). Each pig was allowed 4 weeks to recover before studies commenced.

Study protocol

All studies were performed in unsedated pigs. Each pig was trained to stand quietly in loose fitting slings. Animals were fasted from food for 20 h and from water for 3 h prior to each study.

Prior to the commencement of studies, the stomachs of pigs with gastric cannulae were washed with water at body temperature until the effluent was clear. No differences in either motility patterns or gastric emptying were observed between pigs with oesophageal cannulae (no wash-out) and pigs with gastric cannulae.

Studies were performed with two different manometric assemblies, one assembly used for one study (see below). The manometric assembly was passed through the oesophageal or gastric cannula, to lie at the antro-duodenal region. Correct position of the manometric assembly relative to the pylorus was confirmed by dual point measurement of transmucosal potential difference (see below). A 16-gauge Foley catheter was passed through the duodenal cannula into the second part of the duodenum and its balloon inflated with 5–7 ml of water. This prevented passage of gastric effluent into the second part of the duodenum, directing it instead through the duodenal cannula. The lumen of the Foley catheter was used for infusion of various test solutions into the distal duodenum beyond the balloon. In preliminary studies the effect of inflation of the Foley balloon was investigated in three pigs. Neither emptying of the 5 % dextrose nor manometric patterns were altered by inflation of the Foley balloon to less than 10 ml. When the balloon was inflated beyond 10 ml, suppression of gastric emptying and alteration in the manometric pattern were recorded in each pig.

After passage of the manometric assembly and Foley catheter, manometric recordings were started, concurrent with distal duodenal infusions. Ten minutes following the start of intraduodenal infusion of test solutions, the pig was given a 1000 ml 5 % dextrose drink, labelled with 100 μCi (3·7 MBq) of ^{113m}Indium-DTPA (diethylenetriamine pentaacetate). This was completely drunk by four of the six animals within 2 min. In the remaining two animals, both ingested just over half the drink and the remainder was infused within the first 2 min via a 16-gauge Foley catheter passed through the duodenal cannula into the stomach. Once all the drink was infused, this Foley catheter was removed. No difference was demonstrated in the patterns of either motility or gastric emptying by infusion of part of the drink in this manner.

Multiple side-hole manometric assembly studies. The multiple side-hole studies were done to evaluate the topography of pyloric contractions during intraduodenal infusions of nutrient (dextrose) and non-nutrient (saline) solutions. The catheter assembly incorporated 9 side holes at 6 mm intervals. One study was performed in each of five pigs. For each study, normal saline 20 ml/min was infused intraduodenally for 15 min after ingestion of the 5 % dextrose drink. The intraduodenal infusion was then changed to isosmolar 3·1 % dextrose–saline solution, 20 ml/min which was continued for 15 min. Throughout these infusions, pressures were recorded continuously from all manometric side holes, which were maintained in position astride the pylorus.

Sleeve manometric assembly studies. The assembly incorporated a 5·5 cm sleeve sensor for pyloric manometry and side holes on either side of the sleeve for recording of antral and duodenal pressures. The application of the sleeve sensor to pyloric manometry has been validated in humans (Heddle *et al.* 1988*a*). Studies were performed on six pigs, with eight different infusates tested in each pig, except for one animal in which only four infusates could be tested. In each one test solution was infused continuously for the duration of the study, that is, for 10 min prior and 30 min following ingestion of the radiolabelled 5 % dextrose drink. Test solutions included normal saline as control, isosmolar nutrient solutions of dextrose (31·25 g dextrose plus 3·38 g/l NaCl), amino acids (303 ml/l of Synthamen 17, Travenol), fatty acid (13·9 g/l oleic acid plus 86·1 ml/l NaOH, 0·5 M, plus 9 g/l NaCl) and hyperosmolar solutions of 3 N saline and 25 % dextrose (Table 1). These solutions were chosen to provide a dose-dependent manipulation of the rate of liquid gastric emptying (Landers, Devitt & Jamieson, 1986). Measures of gastric emptying and manometry continued for 30 min following ingestion.

Manometric technique

Each manometric assembly was perfused continuously by a low compliance pneumo-hydraulic capillary infusion system. The pressure rise rate on occlusion at mid-sleeve was 36 mmHg/s and at side-hole occlusion was at least 270 mmHg/s. Pressures were measured by external transducers (two of Gould Statham model P23 1D, Hato Rey, Puerto Rico and seven of Cobe model 01N4655, Lakewood, CO, USA), with output to a 12-channel pen chart polygraph (Grass model 7D polygraph, Quincy, MA, USA), chart speed 100 mm/min. At the start of each study full-scale pen deflection (4 cm) was calibrated at 0–40 mmHg pressure.

The sharp gradient of transmucosal potential difference across the gastro-duodenal junction (Andersson & Grossman, 1965) was used to confirm assembly position (Heddle *et al.* 1988*a*). Side holes at each end of the array of side holes of the multiple side-hole assembly or at each end of the sleeve of the sleeve assembly recorded both intraluminal pressure and transmucosal potential difference, and were referred to as antral and duodenal transmucosal potential difference side holes. Manometric assembly position was adjusted so that antral transmucosal potential difference side-hole readings were more negative than −15 mV and duodenal transmucosal potential difference side-hole readings were less negative than −5 mV. Transmucosal potential difference side holes were perfused by separate saline reservoirs. Transmucosal potential difference was measured through the perfusing saline column, connected via KCl–agar bridges to silver electrodes interfaced to high-impedance purpose-built millivoltmeters (model 1201, Biomedical Engineering, Flinders Medical Centre, South Australia; Geall, Code, McIlrath & Summerskill, 1970). A KCl–agar-filled needle acted as subcutaneous reference. Transmucosal potential difference was monitored on the Grass polygraph. At the start of each study full-scale pen deflection (4 cm) was set at −40 to +40 mV.

Analysis of manometric recordings

Analyses of motility were performed only on those segments of a trace in which transmucosal potential difference criteria confirmed that the manometric assembly was correctly positioned at the gastro-duodenal region. Pressure waves were classified only when equal to or greater than 10 mmHg. Pressure waves were classified either as propagated when onset of the wave in two adjacent side holes differed by at least 0·5 s, or as synchronous (Heddle *et al.* 1988*a*).

Two patterns of pressure waves were recorded and classified (see Results) for sleeve manometric assembly studies: (1) those waves recorded by the sleeve plus one or more side holes proximal to the sleeve of any amplitude were classified as antro-pyloric pressure waves (APWs; Fig. 1*A*); (2) those waves recorded by the sleeve in the absence of pressure waves at any of the side holes proximal or distal to the sleeve were classified at isolated pyloric pressure waves (IPPWs; Heddle *et al.* 1988*a*; Fig. 1*B*). A 'typical sequence' of pressure waves was defined as an episode of three or more of one type of pressure wave, in which the time from onset of any pressure wave to onset of the following pressure wave in that sequence occurred within 20 s.

Pyloric pressure was referenced to antral pressure. Sustained elevations of pyloric pressure (pyloric tone) were expressed at 5 min mean values, derived planimetrically from the traces. Pressure waves were edited by drawing a line from their onset to offset. Abrupt elevations of intraabdominal pressure, caused usually by grunting or body movement, were recognized as they produced identical pressure changes in all manometric channels. Such changes were excluded from analysis.

Measurement of gastric emptying

Prior to each study, a 1 ml sample was taken from the 1000 ml radiolabelled 5% dextrose to be drunk by the pig. This was used to determine the total counts ingested by the pig. Drainage from the duodenal cannula was collected over 5 min intervals, the volume noted and a sample stored for subsequent radio-isotopic counting. The relative volumes of the radiolabelled drink emptied from the duodenal cannula were calculated for each 5 min interval during the 30 min of recording after the dextrose was drunk.

Output from the duodenal cannula was weighed and recorded continuously with a balance interfaced to the polygraph. This allowed measure of rate of flow and correlation of flow with motility. An episode of pulsatile flow was defined as an increase of flow out the cannula of greater than 6 ml/s within a 2 s interval, with a return to the previous rate of flow within the following 20 s. An episode of pulsatile flow was classified as related to a pressure wave when the onset of flow occurred either 8 s before or after onset of a pressure wave recorded by the sleeve sensor. This analysis included an allowance for delay due to the passage of fluid from the duodenal bulb to the cannula and into the collection chamber. This correction factor was determined for each pig by injection of a bolus of fluid into the duodenal bulb. The analysis of pulsatile flow was restricted to sleeve catheter studies which tested the effect of intraduodenal infusion of either normal saline, 20 ml/min or of 3·1% dextrose–saline, 5 ml/min.

Statistical analysis

Statistical analysis was by the Kendall rank correlation coefficient, the Kendall coefficient of concordance and Freidman's test, as appropriate. Differences were considered significance when $P < 0{\cdot}05$.

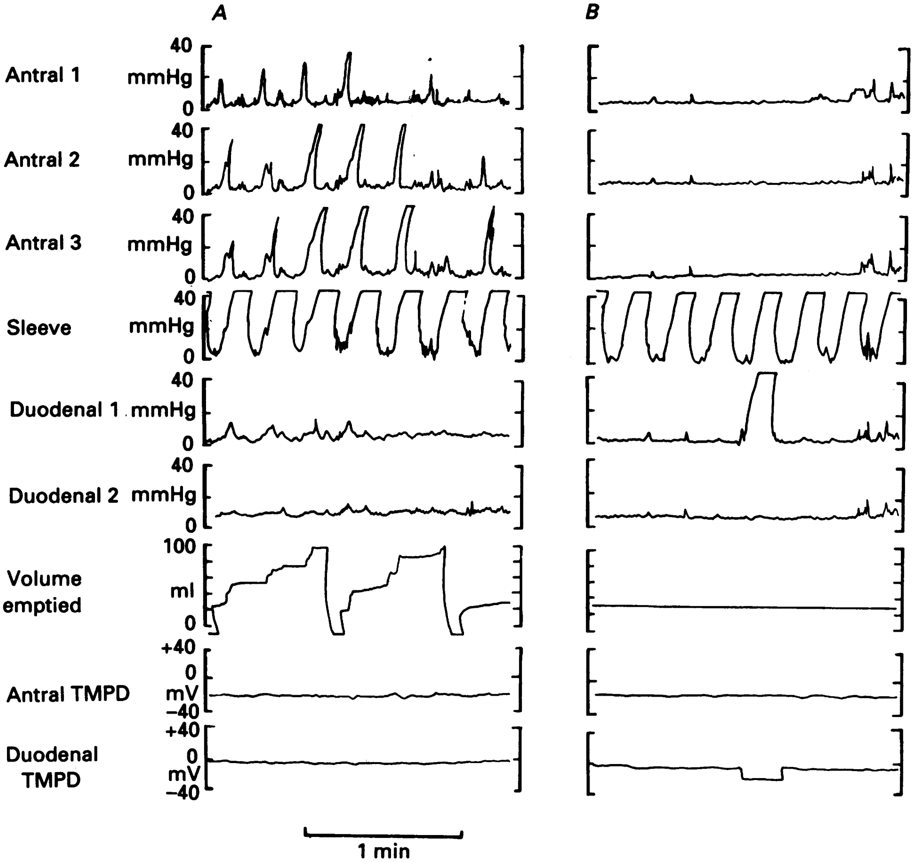

Fig. 1. Characteristic recordings for antro-pyloric pressure waves (*A*) and isolated pyloric pressure waves (*B*). Recordings from one pig during two separate studies. Antral 1, 2 and 3 refers to pressure recordings from the three separate antral side holes. Duodenal 1 and 2 refer to pressure recordings from the two separate duodenal side holes. TMPD refers to transmucosal potential difference recordings. N.B. At one point during the recording of isolated pyloric pressure waves (*B*), the manometric assembly slipped proximally into the stomach and thus out of position, as registered by the duodenal transmucosal potential difference recording. This portion of the recording was edited out.

Ethical approval

The project conformed with the guidelines of the National Health and Medical Research Council of Australia's Statement on Animal Experimentation and was approved in 1986 by the animal ethics committees of the University of Adelaide and the Institute of Medical and Veterinary Science, South Australia.

RESULTS

Topography of pyloric contractions

Two patterns of associated pressure waves were recorded and classified with the multiple side-hole manometric assembly. This classification of pressure waves led to the definitions of antro-pyloric pressure waves (APWs) and isolated pyloric pressure waves (IPPWs) given in the Methods.

During intraduodenal infusion of normal saline, 20 ml/min, fifty-five pressure waves were recorded by the multiple side-hole manometric assembly. Of these, 89% were recorded by seven or more side holes and thus occurred over a length greater than 42 mm. All waves were recorded by the two most proximal side holes of the assembly (at the antrum) and none by the most distal hole of the assembly (at the duodenum). These waves were classified as antro-pyloric pressure waves (APWs). Based on these results, pressure waves recorded with the sleeve manometric assembly were defined as APWs when registered by the sleeve plus one of more side holes proximal to the antral transmucosal potential difference side hole (APW; Fig. 1*A*).

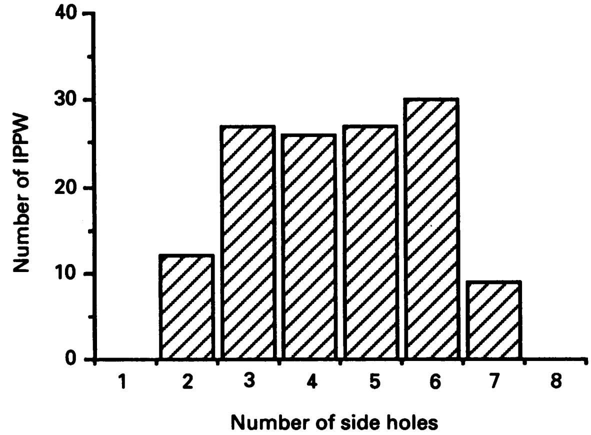

Fig. 2. Width of pyloric phasically active zone. Results from 131 pressure waves recorded by the multiple side-hole manometric assembly during intraduodenal infusion of 3·1% dextrose–saline solution at 20 ml/min. Results from five pigs, one study per pig. N.B. Two side holes demonstrate a possible width of the phasically active zone of between 6–18 mm; three side holes for 12–24 mm; four side holes for 18–30 mm; five side holes for 24–36 mm; six side holes for 30–42 mm; seven side holes for 36–48 mm.

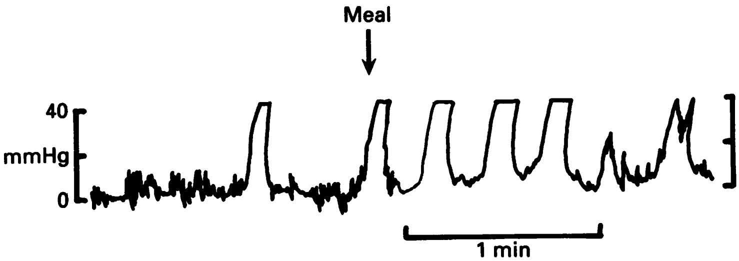

Fig. 3. Stimulation of pyloric motility with ingestion of the 1000 ml radio-labelled 5% dextrose drink. Recording from sleeve sensor, during intraduodenal infusion of 3·1% dextrose–saline solution at 20 ml/min.

The intraduodenal infusion of 3·1% dextrose–saline at 20 ml/min was associated with a second pattern of pressure waves, recorded over a narrow zone at the pylorus alone. Of the 131 pressure waves recorded with the multiple side-hole manometric assembly, 84% were recorded by three to six contiguous side holes and all were recorded by two to seven side holes, that is, the width of the pylorus generating the wave was from a minimum of 12 mm to a maximum of 42 mm in length (Fig. 2). These waves had a synchronous onset across the pylorus and were classified as isolated pyloric pressure waves (IPPWs). Based on this multiple side-hole analysis, pressure waves recorded with the sleeve manometric assembly were defined as IPPWs when registered by the sleeve sensor alone, in the absence of an associated wave of any amplitude at any of the side holes proximal or distal to the sleeve, including the transmucosal potential difference side holes (Fig. 1*B*).

Neither the multiple side-hole nor the sleeve manometric assemblies indicated any sustained elevation in pyloric pressure (pyloric tone) during any study.

Effects of duodenal infusates on antro-pyloro-duodenal motility

Prior to ingestion of the drink, the total number of pressure waves at the pylorus and antrum occurred at an overall median rate of 1·2 waves per minute (Table 1). Ingestion of the drink stimulated the occurrence of regularly occurring pressure waves in all studies, immediately upon presentation of the drink, usually before ingestion had begun (Fig. 3), to an overall rate of 3·1 waves per minute (Table 1).

Following ingestion of the radiolabelled drink, intraduodenal infusion of normal saline was associated with the occurrence of APWs at 1·67 per minute and relative absence of IPPWs at 0·39 per minute (Table 1). Duodenal infusion of dextrose, amino acid, fatty acid and hyperosmolar saline solutions resulted in a markedly different pattern of antro-pyloric motility: IPPWs occurred significantly more frequently; APWs occurred significantly less frequently (Table 1).

The protocol of studies performed with the multiple side-hole manometric assembly permitted examination of the time course of alteration of motility resulting from alteration of duodenal infusate. Conversion from a predominantly APW to a predominantly IPPW pattern occurred 110 s following the change of intraduodenal infusate from saline to dextrose (mean of four pigs, range 40–195 s).

A dose–response relationship was investigated, using differing rates of 3·1% dextrose–saline infusion (Table 1). An increase in the dextrose load infused intraduodenally throughout each study resulted in an significant increase in the rate of IPPW and a significant decrease in the rate of APWs (Table 1).

In all studies, side holes distal to the sleeve, that is, within the duodenum beyond the duodenal cap, did not record any pressure rise, phasic or tonic, except for those due to straining.

Effects of duodenal infusates on gastric emptying

Compared to intraduodenal normal saline infusion, the intraduodenal infusions of dextrose, amino acids, fatty acid and hyperosmolar saline were associated with significant retardation of gastric emptying (Table 1). The volume of the radiolabelled 5% dextrose drink emptied at 30 min decreased in a dose-dependent relationship with delivery of an increasing dextrose calorie load to the duodenum (Table 1), with an 85% concordance between pigs of the volumes emptied.

TABLE 1. Median rates of gastric emptying, isolated pyloric pressure waves (IPPW) and antro-pyloric pressure waves (APW) during sleeve assembly studies

Duodenal infusate	Rate of infusion (ml/min)	Calorie load (kcal/min)	Number of pigs studied	Volume emptied (ml)	Rate of IPPW (per min)		Rate of APW (per min)	
					Fast	Fed	Fast	Fed
Normal saline	20	0	6	739* (642–929)	0·35	0·39†	0·25	1·67‡
3·1 % dextrose	5	0·62	5	553* (359–925)	0·10	0·78†	0·30	0·65‡
3·1 % dextrose	10	1·24	6	507* (107–765)	0·65	0·85†	0	0·82‡
3·1 % dextrose	20	2·48	6	72*§ (6–332)	1·25	2·98†§	0·15	0·12‡§
Amino acids	30	3·72	5	104§ (8–736)	0·70	1·00§	0·10	0·19§
Fatty acid	5	0·62	5	46§ (13–128)	0·70	1·02§	0·40	0·59§
3 N saline	10	0	5	190§ (0–236)	0·80	1·49§	0·40	0·18§
25 % dextrose	4	4·00	6	51§ (0–236)	1·00	2·74§	0·20	0§

* $P < 0{\cdot}05$, correlation gastric emptying with duodenal calorie load.

† $P < 0{\cdot}05$, correlation IPPW with duodenal calorie load.

‡ $P < 0{\cdot}05$, correlation APW with duodenal calorie load.

§ $P < 0{\cdot}05$, *versus* saline infusion.

Fast = prior to ingestion; Fed = following ingestion. Ranges in parentheses.

Relationship between gastric emptying and antro-pyloro-duodenal motility

Fifty-three typical sequences of IPPWs were recorded, during intraduodenal infusion of nutrient or hyperosmolar solutions. Transpyloric flow occurred during these sequences at a median of 4·7 ml/min (range 0–35 ml/min).

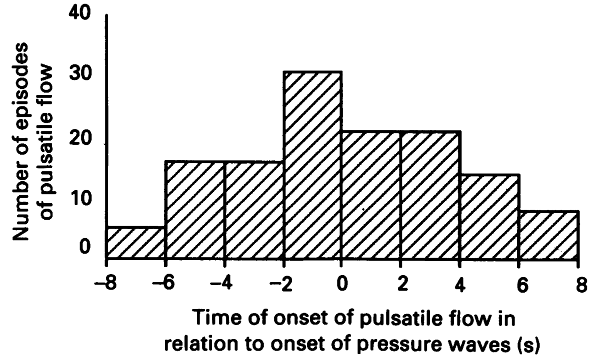

Fig. 4. Timing of episodes of pulsatile flow in relation to antro-pyloric pressure waves (APW). Results from 137 pressure waves recorded by the sleeve sensor in six pigs. Negative value means flow occurred before onset of pressure wave at sleeve sensor.

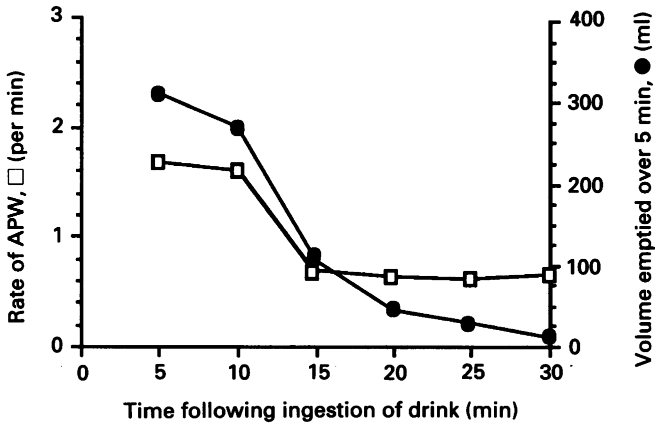

Fig. 5. Relationship between rate of antro-pyloric pressure waves (APW) and volume of drink emptied, during normal saline infusion, each 5 min interval of a study. Results from six pigs, one study per pig.

Episodes of strictly defined pulsatile flow accounted for 52% of the total volume emptied from the stomach, with a mean volume of each episode of 16·2 ml (range 4–70 ml). Of the 150 episodes of pulsatile flow recorded, 91% (137) were related to an APW, occurring 0·9 ± 4·9 s prior to the onset of a sleeve-recorded pressure wave (Fig. 4). Only 31% (137 out of 435) of the APWs recorded were associated with a clearly defined episode of pulsatile flow. Pulsatile flow associated with APWs occurred at 57 ml/min (range 14–240 ml/min). The rate of APWs paralleled the rate of gastric emptying of the radiolabelled drink over each 5 min interval of each study, whether emptying occurred exponentially as during normal saline infusion (Fig. 5), or more linearly as during 3·1% dextrose–saline infusions at 5 and 10 ml/min (Fig. 6). The volume of each episode of pulsatile flow related to an APW correlated with the extent of the antro-pyloric segment over which the APW occurred, as measured by the number of antro-pyloric side holes which registered the pressure wave ($P = 0{\cdot}001$).

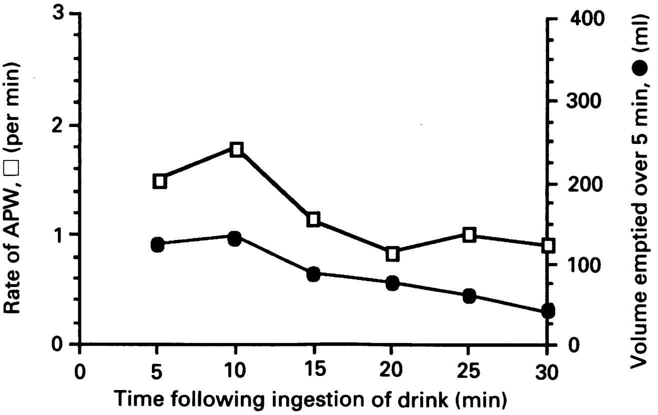

Fig. 6. Relationship between rate of antro-pyloric pressure waves (APW) and volume of drink emptied, during intraduodenal 3·1% dextrose–saline infusion at 5 and 10 ml/min, each 5 min interval of a study. Results from six pigs, two studies per pig.

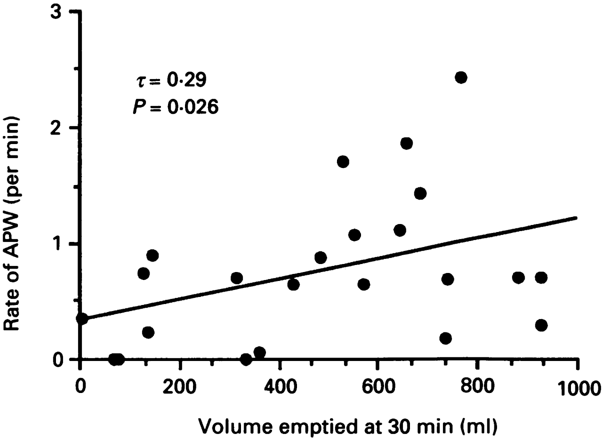

Fig. 7. Correlation between gastric emptying and rate of antro-pyloric pressure waves (APW). Results from six pigs, four studies each pig (three only in one pig), during intraduodenal infusion of saline or 3·1% dextrose–saline solutions.

In the post-prandial period, periods of motor quiescence of greater than 1 min duration were recorded only 8% of the time in total. This absence of activity was seen in only twenty-two out of the total forty-four studies with the sleeve manometric assembly. During these periods, flow occurred at a median rate of 20·1 ml/min (range 2·5–46·0 ml/min). No relation was demonstrated between emptying and type of infusate during these periods of quiescence (P = n.s.). During these periods of motor quiescence no pulsatile flow was recorded.

In studies with intraduodenal infusion of 3·1% dextrose–saline, there was a statistically significant positive correlation between emptying of the radiolabelled drink and the rate of APWs (Fig. 7) and a significant negative correlation between emptying and the rate of IPPW (Fig. 8). Concordance of the rates of IPPWs between pigs was 66% and of the rates of APWs was 60%.

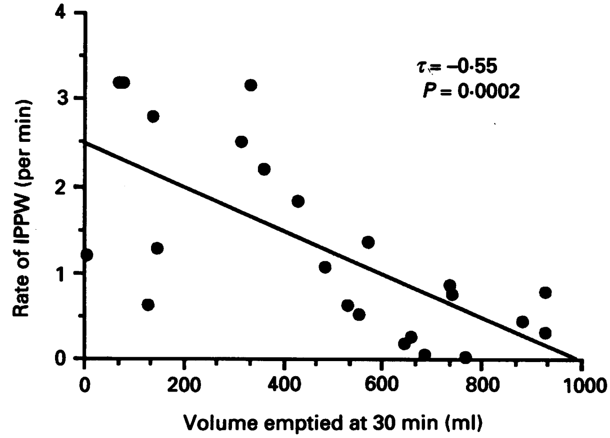

Fig. 8. Correlation between gastric emptying and rate of isolated pyloric pressure waves (IPPW). Results from six pigs, four studies each pig (three only in one pig), during intraduodenal infusion of normal saline or 3·1% dextrose–saline solutions.

DISCUSSION

This study gives new information about the mechanical factors that control gastric emptying of liquids. These insights have been possible because the technique used has allowed recordings of detailed patterns of antro-pyloric motility in association with close correlation of timing of emptying of liquids into the duodenum. The major findings are: (1) that isolated pyloric pressure waves (IPPWs) are closely associated with cessation of transpyloric flow of liquids; (2) that more than half of liquid emptying occurs as episodes of pulsatile flow, which are intimately associated in time with antro-pyloric pressure waves (APWs); (3) that IPPWs are stimulated and antral pressure waves are inhibited by the intraduodenal infusion of a range of nutrient and hyperosmolar solutions (in the case of intraduodenal dextrose infusion, a dose–response relationship was investigated and demonstrated); (4) that the nutrient and hyperosmolar stimulation of receptors within the proximal small intestine results in very potent retardation of gastric emptying of liquids. In the case of intraduodenal dextrose infusion, a dose-related retardation of gastric emptying was investigated and demonstrated.

This study has demonstrated a close association between IPPWs and cessation of gastric emptying of liquids in two ways. First, a positive correlation was demonstrated between rates of IPPWs and retardation of gastric emptying over the 30 min duration of each study. Second, near cessation of transpyloric flow was recorded during individual sequences of IPPWs within one study. These associations support the hypothesis that IPPWs and retardation of gastric emptying are causally linked, that is, that IPPWs obstruct liquid gastric emptying. How can IPPWs obstruct transpyloric flow, when no pyloric pressure gradient exists between each phasic pressure wave of a sequence of IPPWs? We believe the interval between each IPPW, when pyloric pressure equals antral pressure, is too brief for the pylorus to open and much flow to be established. Further studies utilizing concurrent manometry with fluoroscopic imaging might help resolve this issue. Low-amplitude pyloric tone may have occurred, but could not be resolved because of the practical difficulties of resolving small pressures caused by animal movement, straining and grunting.

The hypothesis that IPPWs are obstructive to liquid gastric emptying is supported by findings from other studies. A pattern of non-propagated pressure waves localized to the pylorus has been demonstrated in humans (White, Poxon & Alexander-Williams, 1981; Heddle *et al.* 1988*a*). These waves are stimulated by the intraduodenal infusion of various nutrient solutions (Fisher & Cohen, 1973; White, Poxon & Alexander-Williams, 1983; Heddle, Dent, Read, Houghton, Toouli, Horowitz, Maddern & Downton, 1988*b*; Heddle, Fone, Dent, Horowitz, 1988*c*). Such localized pyloric contractions have been shown to occur more frequently during slowing of gastric emptying (Houghton, Read, Heddle, Maddern, Downton, Toouli & Dent, 1988), by the normal feedback inhibition of gastric emptying (Collins, Horowitz, Cook, Harding & Shearman, 1983). IPPWs have also been demonstrated radiologically to be associated with obstruction of transpyloric flow (Tougas, Anvari, Richards, Dent, Somers & Stevenson, 1987). These studies support the findings original to our study, that the latencies, thresholds and magnitudes of retardation of gastric emptying, measured directly, are closely if not causally associated with IPPWs.

Ehrlein and co-workers have similarly studied motor activity of the distal stomach, using extraluminal induction coils combined with radio-isotopic imaging of gastric emptying. Findings from Ehrlein's studies are largely in agreement with this study. Ehrlein reported that after meals 'the external pyloric diameter increased and decreased in the rhythm of the antral waves; that is, the pylorus opened and closed rhythmically' (Ehrlein, 1988). This motor pattern corresponds with antro-pyloric pressure waves. Ehrlein also reported continued motor activity of the pylorus in the absence of antral activity. Intraduodenal oleic acid 'delayed gastric emptying and diminished to a variable extent antral and duodenal motility as well as the pyloric opening' (Keinke, Schemann & Ehrlein, 1984). These changes are consistent with the motor pattern of isolated pyloric pressure waves we report. Induction coils, as used by Ehrlein and co-workers, signal the pyloric diameter and are not an effective method of recognizing a sequence of isolated pyloric pressure waves, as during the marked phasic pressure changes of IPPWs, the pyloric lumen rarely opens (Gershon-Cohen, Shay & Fels, 1937; Tougas *et al.* 1987; White *et al.* 1983). The conclusion by Ehrlein that 'relaxation of the pyloric sphincter is more an isotonic than an isometric phenomenon' (Keinke *et al.* 1984) is not necessarily correct. Although pyloric tone was not recorded in the pig studies, pyloric tone has been recorded with intraluminal manometric techniques in other animal preparations (Brink, Schlegel & Code, 1965;

Isenberg & Csendes, 1972; Bertiger, Reynolds, Ouyang & Cohen, 1987) and in man (Fisher & Cohen, 1973; Valenzuela, Defilippi & Csendes, 1976; Phaosawasdi & Fisher, 1982). The absence of tone in the pig preparation may reflect species difference.

In this study, when duodenal stimulation was minimal or absent, at least half of liquid emptying occurred as pulsatile episodes, which were closely associated in time with APW. This observation emphasizes the importance of antral pumping as a normal mechanism of gastric emptying. Flow commencing *before* a pressure wave was classified as related to that wave, as timing was related to onset of the wave recorded at the pylorus. The more proximal antrum may have contracted earlier than the pylorus, or contraction have commenced but been non-lumen-occluding initially, and so not initially recorded. Fluid pulses presumably travel in advance of an antral pump contraction.

Detailed analysis of our data on the frequency and volume of episodes of pulsatile flow indicate a possible mechanism for fine tuning of the antral pump. The frequency of APWs paralleled the rate of gastric emptying, whether emptying was linear or exponential. Also, a direct relationship existed between the volume of each episode of pulsatile flow and the extent of the antro-pyloric segment over which the pressure wave was recorded. It may be concluded that the volume emptied as pulses was modulated by both contraction rate and stroke volume of the antro-pyloric segment. However, this may represent an effect rather than a cause. It may be that during more rapid gastric emptying, larger volumes of fluid entered the distal stomach, which stretched the antro-pyloric segment to a greater extent and so provoked a more extensive contraction of the antro-pyloric segment.

Intermittency of forward transpyloric flow has been recognized previously, with real-time ultrasonography (King, Adam, Pryde, McDicken & Heading, 1984), fluoroscopic observations of barium emptying (Carlson, Code & Nelson, 1966) and radio-isotopic imaging of semi-solids (Jacobs, Akkermans, Yoe, Hoekstra & Wittebol, 1982). However, none of these techniques allowed measurement of individual pulse volumes and the proportion of gastric emptying that occurred in flow pulses. The methods used in the present study have allowed this to be done and have shown that pulsatile emptying is quantitatively important.

Prior to ingestion, pyloric pressure waves were infrequent, occurring at a rate about one-half the rate that occurred after ingestion. In other words motility of the pylorus was not omnipresent, but was stimulated by ingestion of the drink. It was stimulated further by nutrient or hyperosmolar infusions into the duodenum. Stimulation following ingestion may occur in response to the cephalic stimuli of sight, smell and taste of food, or to distension of the stomach by the ingested meal. That regular unrelenting pressure waves commenced within seconds of presentation of the meal to the animal, often before drinking had begun and always before any significant volume of the drink had entered the stomach, suggests a major role for cephalic mechanisms, and warrants further study. Sham feeding had been attempted in a few preliminary studies, but was abandoned as the animals became uncontrollable when food was withheld.

That periods of motor quiescence were recorded confirms that IPPWs do not arise merely by inhibition of antral contractions with continuation of pyloric contractions.

IPPWs are stimulated to occur. During post-prandial periods of motor quiescence, emptying occurred at a rate intermediate between that of pulsatile flow associated with APWs and flow during typical sequences of IPPWs. When IPPWs recommenced, emptying slowed. This supports our hypotheses that IPPWs *per se* produce retardation of gastric emptying and that antral pumping is an important mechanism in the promotion of liquid gastric emptying. We propose that retardation of liquid gastric emptying is achieved through an orderly series of processes, involving removal of antral pumping, followed by stimulation of pyloric resistances through IPPWs.

As gastric emptying, albeit slow and non-pulsatile, was observed in the absence of any antral or pyloric motor activity, this suggests that other motor mechanisms, such as proximal gastric tone, may act to promote gastric emptying. This study has not evaluated the role of the proximal stomach nor variations in intragastric volume. Further experiments are needed to define their relative importance in relation to the effects observed. Rees, Go & Malagelada (1979) also noted slow gastric emptying in the absence of antral contractions, measured in humans by radio-isotopic imaging. However the methods used by Rees *et al.* (1979) did not allow accurate recording of pyloric motility nor detailed analyses of timing of flow. Gastric emptying independent of the proximal stomach has been observed by others, using a gastric barostat system (Miller, Kauffman, Elashoff, Ohashi, Carter & Meyer, 1981; Williams, Miller, Elashoff & Meyer, 1986).

This study has confirmed a very potent retardation of gastric emptying of liquids, by the nutrient or hyperosmolar stimulation of receptors within the proximal small intestine. The responses were identical for each stimulus tested. This suggests that one final common pathway is involved in the entero-gastric feedback control of motility and emptying. The variables of osmolarity, calorie load and nature of infusate were not held constant in such a way that allows comparison of the effects of osmolarity or calorie in their own right. If one considers that each isosmolar solution (3·1% dextrose–saline, calorie load 2·48 kcal/min, fatty acid, calorie load 0·62 kcal/min and amino acids solution, calorie load 3·72 kcal/min) produced an equivalent retardation of gastric emptying (Table 1), one may conclude that retardation of gastric emptying, calorie for calorie, was greatest for fatty acid, intermediate for dextrose and least for amino acids solution.

In the present study no motor activity was recorded from the duodenum beyond the duodenal cap. We believe this is due to drainage of this part of the duodenum by the duodenal cannula, and that as a result duodenal resistances were minimal, as proposed by Parr, Grime, Baxter, Critchley & Mackie (1987). Exclusion of duodenal factors allowed more conclusive demonstration of the obstructive nature of IPPWs than was possible in the radiological study on humans by Tougas *et al.* (1987), in which duodenal resistances could not be excluded.

The experimental approach taken in this study was designed to allow measurements in awake unsedated animals. The study of awake animals is important, since higher centres are known to exert important controls on gastric emptying, from stimuli such as acute stress (Thompson, Richelson & Malagelada, 1983). Our experience with the sleeve manometric assembly indicates that it is a useful technique for obtaining prolonged recordings of pyloric function in awake animals.

The establishment of this capability holds promise for better definition of the mechanical roles and control of the pylorus, given the potential for experimental manipulation of sensory and motor control pathways as well as alterations of pyloric mechanics in such a model.

The pig pylorus is not an exact mimic of that of the human. In humans IPPWs occur in a segment usually less than 9 mm in width (Heddle *et al.* 1988*a*), whilst the multiple side-hole manometric analysis performed in the present study showed that IPPWs occurred over a greater luminal length, of between 12 and 42 mm. Torgersen (1942) recognized anatomically the greater length of the pyloric segment in the pig than in humans. Pyloric tone was not demonstrated in the present study, in contrast to results in humans (Heddle *et al.* 1988*a*, *b*, *c*). Despite these differences, there is a very close similarity in the mechanical patterns of IPPWs and the stimuli that produce them, in humans and pigs.

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